

FIG. 1A

Heavy Chain IgG1 Constant Region

gcctccacca	agggcccatc	ggtcttcccc	ctggcaccct	cctccaagag	cacctctggg	60
ggcacagcgg	ccctgggctg	cctgggtcaag	gactacttcc	ccgaaccggg	gacgggtgctg	120
tggaaactcag	gcgccctgac	cagcggcgtg	cacaccttcc	cggctgtcct	acagtcctca	180
ggactctact	ccctcagcag	cgtgggtgacc	gtgccctcca	gcagcttggg	caccagacc	240
tacatctgca	acgtgaatca	caagcccagc	aacaccaagg	tggacaagaa	agttgagccc	300
aaatcttggt	acaaaactca	cacatgcccc	ccgtgcccag	cacctgaact	cctgggggga	360
ccgtcagtct	tctcttcccc	cccaaaaccc	aaggacaccc	tcatgatctc	ccggaccctt	420
gaggtcacat	gcgtgggtgt	ggacgtgagc	cacgaagacc	ctgaggtcaa	gttcaactgg	480
tacgtggacg	gcgtggaggt	gcataatgcc	aagacaaagc	cgcgggagga	gcagtacaac	540
agcacgtacc	gtgtgggtcag	cgtcctcacc	gtcctgcacc	aggactgggt	gaatggcaag	600
gagtacaagt	gcaaggtctc	caacaaagcc	ctcccagccc	ccatcgagaa	aaccatctcc	660
aaagccaaag	ggcagccccg	agaaccacag	gtgtacaccc	tgcccccatc	ccgggatgag	720
ctgaccaaga	accaggtcag	cctgacctgc	ctgggtcaaag	gcttctatcc	cagcgacatc	780
gccgtggagt	gggagagcaa	tgggcagccg	gagaacaact	acaagaccac	gcctcccgtg	840
ctggactccg	acggctcctt	cttcctctat	agcaagctca	ccgtggacaa	gagcaggtgg	900
cagcagggga	acgtcttctc	atgctccgtg	atgcatgagg	ctctgcacaa	ccactacacg	960
cagaagagcc	tctccctgtc	tccgggtaaa				990

FIG. 1B

ASTKGPSVFP	LAPSSKSTSG	GTAALGCLVK	DYFPEPVTVS	WNSGALTSGV	HTFPAVLQSS	60
GLYSLSSVVT	VPSSSLGTQT	YICNVNHNKPS	NTKVDKKVEP	KSCDKTHTCP	PCPAPELLGG	120
PSVFLFPPKP	KDTLMISRTP	EVTCVVVDVS	HEDPEVKFNW	YVDGVEVHNA	KTKPREEQYN	180
STYRVVSVLT	VLHQDWLNGK	EYKCKVSNKA	LPAPIEKTIS	KAKGQPREPQ	VYTLPPSRDE	240
LTKNQVSLTC	LVKGFYPSTI	AVEWESNGQP	ENNYKTTTPV	LDSDGSFFLY	SKLTVDKSRW	300
QQGNVFSCSV	MHEALHNHYT	QKSLSLSPGK				330

FIG. 2A

Kappa Chain Constant Region

cgaactgtgg	ctgcaccatc	tgtcttcac	ttcccgccat	ctgatgagca	gttgaaatct	60
ggaactgcct	ctgttggtg	cctgctgaat	aacttctatc	ccagagaggc	caaagtacag	120
tggaagggtg	ataacgccct	ccaatcgggt	aactcccagg	agagtgtcac	agagcaggac	180
agcaaggaca	gcacctacag	cctcagcagc	accctgacgc	tgagcaaagc	agactacgag	240
aaacacaaaag	tctacgcctg	cgaagtcacc	catcagggcc	tgagctcgcc	cgtcacaaaag	300
agcttcaaca	ggggagagtg	t				321

FIG. 2B

RTVAAPSVFI	FPPSDEQLKS	GTASVVCLLN	NFYPREAKVQ	WKVDNALQSG	NSQESVTEQD	60
SKDSTYSLSS	TLTLKADYE	KHKVYACEVT	HQGLSSPVTK	SFNRGEC		107

FIG. 3A

Heavy Chain IgG2 Constant Region

gcctccacca	agggcccatc	ggtcttcccc	ctggcgccct	gctccaggag	cacctccgag	60
agcacagcgg	ccctgggctg	cctgggtcaag	gactacttcc	ccgaaccggt	gacggtgtcg	120
tggaactcag	gcgctctgac	cagcggcggtg	cacaccttcc	cagctgtcct	acagtcctca	180
ggactctact	ccctcagcag	cgtgggtgacc	gtgccctcca	gcaacttcgg	cacccagacc	240
tacacctgca	acgtagatca	caagcccagc	aacaccaagg	tggacaagac	agttgagcgc	300
aaatgttggtg	tcgagtgtccc	accgtgtccc	gcaccacctg	tggcaggacc	gtcagtcttc	360
ctcttcccc	caaaacccaa	ggacaccctc	atgatctccc	ggaccctga	ggtcacgtgc	420
gtggtggtgg	acgtgagcca	cgaagacccc	gaggtccagt	tcaactggta	cgtggacggc	480
gtggaggtgc	ataatgccaa	gacaaagcca	cgggaggagc	agttcaacag	cacgttcctg	540
gtggtcagcg	tcctcaccgt	tgtgcaccag	gactggctga	acggcaagga	gtacaagtgc	600
aaggtctcca	acaaaggcct	cccagcccc	atcgagaaaa	ccatctccaa	aaccaaggga	660
cagccccgag	aaccacaggt	gtacaccctg	ccccatccc	gggaggagat	gaccaagaac	720
caggtcagcc	tgacctgcct	ggtcaaaggc	ttctacccca	gcgacatcgc	cgtggagtgg	780
gagagcaatg	ggcagccgga	gaacaactac	aagaccacac	ctcccatgct	ggactccgac	840
ggctccttct	tcctctacag	caagctcacc	gtggacaaga	gcaggtggca	gcaggggaac	900
gtcttctcat	gctccgtgat	gcatgaggct	ctgcacaacc	actacacgca	gaagagcctc	960
tcctgtctc	cgggtaaa					978

FIG. 3B

ASTKGPSVFP	LAPCSRSTSE	STAALGCLVK	DYFPEPVTVS	WNSGALTSGV	HTFPAVLQSS	60
GLYSLSSVVT	VPSSNFGTQT	YTCNVDHKPS	NTKVDTKVER	KCCVECPCP	APPVAGPSVF	120
LFPKPKDTL	MISRTPEVTC	VVVDVSHEDP	EVQFNWYVDG	VEVHNAKTKP	REEQFNSTFR	180
VVSVLTVVHQ	DWLNGKEYKC	KVSNKGLPAP	IEKTISKTKG	QPREPQVYTL	PPSREEMTKN	240
QVSLTCLVKG	FYPSTIAVEW	ESNGQPENNY	KTTTPMLDSD	GSFFLYSKLT	VDKSRWQQGN	300
VFSCSVMHEA	LHNHYTQKSL	SLSPGK				326

FIG. 4A

Heavy Chain IgG4 Constant Region

gccagcacca	agggggccatc	cgtcttcccc	ctggcgccct	gctccaggag	cacctccgag	60
agcacagccg	ccctgggctg	cctgggtcaag	gactacttcc	ccgaaccggt	gacggtgtcg	120
tggaactcag	gcgccctgac	cagcggcggtg	cacaccttcc	cggctgtcct	acagtcctca	180
ggactctact	ccctcagcag	cgtgggtgacc	gtgccctcca	gcagcttggg	cacgaagacc	240
tacacctgca	acgtagatca	caagcccagc	aacaccaagg	tggacaagag	agttgagtc	300
aaatatggtc	ccccatgccc	atcatgccc	gcacctgagt	tcctgggggg	accatcagtc	360
ttcctgttcc	ccccaaaacc	caaggacact	ctcatgatct	cccggacccc	tgaggtcacg	420
tgcgtgggtg	tggacgtgag	ccaggaagac	cccagggtcc	agttcaactg	gtacgtggat	480
ggcgtggagg	tgcataatgc	caagacaaaag	ccgcggggagg	agcagttcaa	cagcacgtac	540
cgtgtgggtca	gcgtcctcac	cgtcctgcac	caggactggc	tgaacggcaa	ggagtacaag	600
tgcaaggtct	ccaacaaaag	cctcccgtcc	tccatcgaga	aaaccatctc	caaagccaaa	660
gggcagcccc	gagagccaca	ggtgtacacc	ctgcccccat	cccaggagga	gatgaccaag	720
aaccagggtca	gcctgacctg	cctgggtcaaa	ggcttctacc	ccagcgacat	cgccgtggag	780
tgggagagca	atgggagacc	ggagaacaac	tacaagacca	cgcctcccgt	gctggactcc	840
gacggctcct	tcttcctcta	cagcaggcta	accgtgraca	agagcagggtg	gcaggagggg	900
aatgtcttct	catgctccgt	gakgcatgag	gctctgcaca	accactacac	acagaagagc	960
ctctccctgt	ctctgggtaa	a				981

FIG. 4B

ASTKGPSVFP	LAPCSRSTSE	STAALGCLVK	DYFPEPVTVS	WNSGALTSGV	HTFPAVLQSS	60
GLYSLSSVVT	VPSSSLGTKT	YTCNVDHKPS	NTKVDKRVES	KYGPPCPSCP	APEFEGGPSV	120
FLFPPKPKDT	LMISRTPEVT	CVVVDVSQED	PEVQFNWYVD	GVEVHNAKTK	PREEQFNSTY	180
RVVSVLTVLH	QDWLNGKEYK	CKVSNKGLPS	SIEKTISKAK	GQPREPQVYT	LPPSQEEMTK	240
NQVSLTCLVK	GFYPDSIAVE	WESNGQPENN	YKTPPVLDL	DGSFFLYSRL	TVDKSRWQEG	300
NVFSCSVMHE	ALHNHYTQKS	LSLSLGK				327

FIG. 5A

26F5 Heavy Chain

atggagtttg	ggctgagctg	ggtcttcctc	gttgctcttt	taagaggtgt	ccagtgtcag	60
gtgcagctgg	tggagtctgg	gggagggcgtg	gtccagcctg	ggaggtccct	gagactctcc	120
tgtgcagcgt	ctggattcac	cttcagcaac	tatggcatgc	actgggtccg	ccaggctcca	180
ggcaaggggc	tggagtgggt	ggcaggcatt	tggaatgatg	gaattaataa	ataccatgca	240
cactccgtga	ggggccgatt	caccatctcc	agagacaatt	ccaagaacac	gctgtatctg	300
caaatgaaca	gcccgagagc	cgaggacacg	gctgtgtatt	actgtgcgag	agcacggtct	360
ttcgactggc	tattatttga	gttctggggc	cagggaaacc	tggtcacctg	ctctagt	417

FIG. 5B

MEFGLSWVFL	VALLRGVQCQ	VQLVESGGGV	VQPGRSLRLS	CAASGFTFSN	YGMHWVRQAP	60
GKGLEWVAGI	WNDGINKYHA	HSVRGRFTIS	RDNSKNTLYL	QMNSPRAEDT	AVYYCARARS	120
FDWLLFEFWG	QGTTLTVSS					139

FIG. 6A

26F5 Kappa Chain

atggaagccc	cagctcagct	tctcttcctc	ctgctactct	ggctcccaga	taccaccgga	60
gaaatttgtgt	tgacacagtc	tccagccacc	ctgtctttgt	ctccagggga	aagagccacc	120
ctctcctgca	gggccagtc	gagtggttagc	agctacttag	cctgggtacca	acagaaacct	180
ggccaggctc	ccaggctcct	catctatgat	gcaccaaca	gggccactgg	catcccagcc	240
aggttcagtg	gcagtgggtc	tgggacagac	ttcactctca	ccatcagcag	cctagagcct	300
gaagattttg	cagtttatta	ctgtcagcag	cgtagcaact	ggcctccgct	cactttcggc	360
ggagggacca	aggtggagat	caaa				384

FIG. 6B

MEAPAQLLFL	LLLWLPDTTG	EIVLTQSPAT	LSLSPGERAT	LSCRASQSVS	SYLAWYQQKP	60
GQAPRLLIYD	ASNRATGIPA	RFSGSGSGTD	FTLTISLEP	EDFAVYQCQ	RSNWPPLTFG	120
GGTKVEIK						128

FIG. 7A

27F2 Heavy Chain

atggagtttg	ggctgagctg	ggttttcctc	gttgcctctt	taagaggtgt	ccagtgtcag	60
gtgcagctgg	tggagtctgg	gggaggcgtg	gtccagcctg	ggaggtcctt	gagactctcc	120
tgtgcagtgt	ctggattcac	cttcagtaac	tatggcatgc	actgggtccg	ccaggctcca	180
ggcaaggggc	tggagtgggt	ggcagctata	tggaatgatg	gagaaaataa	acaccatgca	240
ggctccgtga	ggggccgatt	caccatctcc	agagacaatt	ccaagaacac	gctgtatctg	300
caaatgaaca	gcctgagagc	cgaggacacg	gctgtgtatt	actgtgcgag	aggacgatat	360
tttgactggt	tattatttga	gtattggggc	cagggaaccc	tggtcacctg	ctctagt	417

FIG. 7B

MEFGLSWVFL	VALLRGVQCQ	VQLVESGGGV	VQPGRSLRLS	CAVSGFTFSN	YGMHWVRQAP	60
GKGLEWVAAI	WNDGENKHHA	GSVRGRFTIS	RDNSKNTLYL	QMNSLRAEDT	AVYYCARGRY	120
FDWLLFEYWG	QGTILVTVSS					139

FIG. 8A

15C4 Heavy Chain

atggggtcaa	ccgccatcct	cgccctcctc	ctggctgttc	tccaaggagt	ctgtgccgag	60
gtgcagctga	tgcagtctgg	agcagaggtg	aaaaagcccg	gggagtctct	gaagatctcc	120
tgtaagggtt	ctggatacag	cttttccttc	cactggatcg	cctgggtgcg	ccagatgccc	180
gggaaaggcc	tggagtggat	ggggatcatc	catcctgggtg	cctctgatac	cagatacagc	240
ccgtccttcc	aaggccaggt	caccatctca	gccgacaact	ccaacagcgc	cacctacctg	300
cagtggagca	gcctgaaggc	ctcggacacc	gccatgtatt	tctgtgcgag	acaaagggaa	360
ctcgactact	ttgactactg	gggccaggga	accctgggtca	ccgtctctag	t	411

FIG. 8B

MGSTAILALL	LAVLQGVCAE	VQLMQSGAEV	KKPGESLKIS	CKGSGYSFSF	HWIAWVRQMP	60
GKGLEWMGII	HPGASDTRYs	PSFQGQVTIS	ADNSNSATYL	QWSSLKASDT	AMYFCARQRE	120
LDYFDYWGGQ	TLVTVSS					137

FIG. 9A

15C4 Kappa Chain

atgtcgccat	cacaactcat	tgggtttctg	ctgctctggg	ttccagcctc	caggggtgaa	60
attgtgctga	ctcagtctcc	agactttcag	tctgtgactc	caaaggagaa	agtcaccatc	120
acctgccggg	ccagtcagag	cattggtagt	agcttacact	ggtagcagca	gaaaccagat	180
cagtctccaa	agctcctcat	caagtatgct	tcccagtcct	tctcaggggt	cccctcgagg	240
ttcagtggca	gtggatctgg	gacagatttc	accctcacca	tcaatagcct	ggaagctgaa	300
gatgctgcag	cgtattactg	tcatcagagt	agtagtttac	ctctcacttt	cggcggaggg	360
accaagggtg	agatcaaa					378

FIG. 9B

MSPSQLIGFL	LLWVPASRGE	IVLTQSPDFQ	SVTPKEKVTI	TCRASQSIGS	SLHWYQQKPD	60
QSPKLLIKYA	SQSFSGVPSR	FSGSGSGTDF	TLTINSLEAE	DAAAYYCHQS	SSLPLTFGGG	120
TKVEIK						126

FIG. 10

				CDR1		CDR2
26F5	QVQLVESGGG	VVQPGRSLRL	SCAASGFTFS	<u>NYGMHWVRQA</u>	PGKGLEWVAG	<u>IWNDGINKYH</u>
27F2	QVQLVESGGG	VVQPGRSLRL	SCAVSGFTFS	<u>NYGMHWVRQA</u>	PGKGLEWVAA	<u>IWNDGENKHH</u>
15C4	EVQLMQSGAE	VKKPGESLKI	SCKGSGYSFS	<u>FHWIAWVRQM</u>	PGKGLEWMI	<u>IHPGASDTRY</u>
						CDR3
26F5	<u>AHSVRGRFTI</u>	SRDNSKNTLY	LMNSPRAED	TAVYYCARAR	SFDWLLFEFW	GQGLVTVSS
27F2	<u>AGSVRGRFTI</u>	SRDNSKNTLY	LMNSLRAED	TAVYYCARGR	YFDWLLFEYW	GQGLVTVSS
15C4	<u>SPSFQGQVTI</u>	SADNSNSATY	LQWSSLKASD	TAMYFCARQR	<u>ELDYFDYWGQ</u>	GTLVTVSS

FIG. 11

	CDR1
26F5/27F2	EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLAWYQOKP GQAPRLLIYD
15C4	EIVLTQSPDF QSVTPKEKVT ITCRASQSIG SSLHWYQOKP DQSPKLLIKY

	CDR2	CDR3
26F5/27F2	ASNRATGIPA RFSGSGSGTD FTLTISSLEP EDFAVYYCQQ RSNWPPLTFG	
15C4	ASQSFSGVPS RFSGSGSGTD FTLTINSLEA EDAAAYYCHO SSSLPLTFGG	

26F5/27F2	GGTKVEIK
15C4	GTKVEIK

FIG. 12

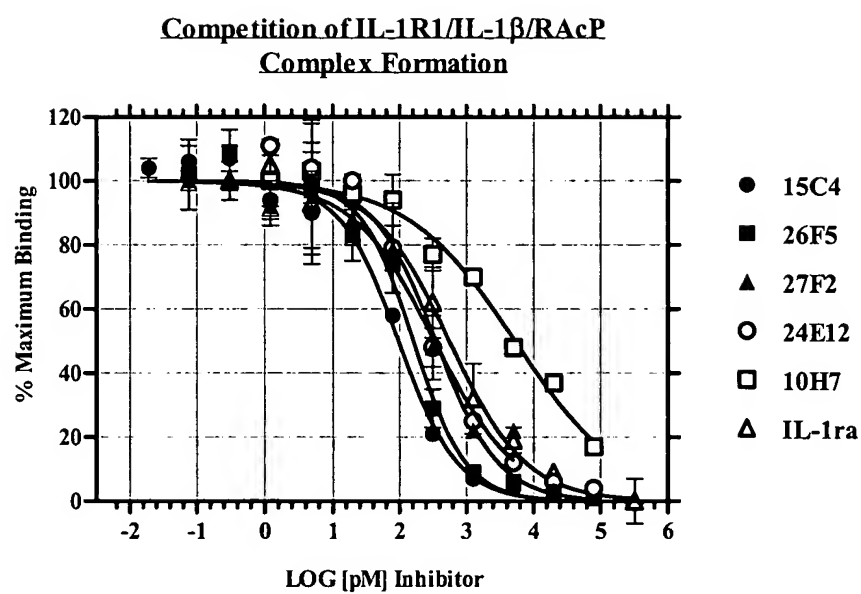


FIG. 13

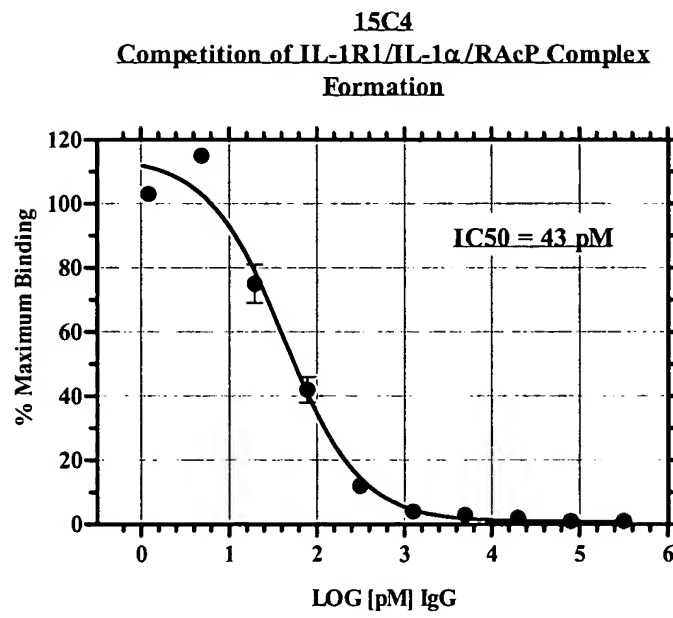


FIG. 14

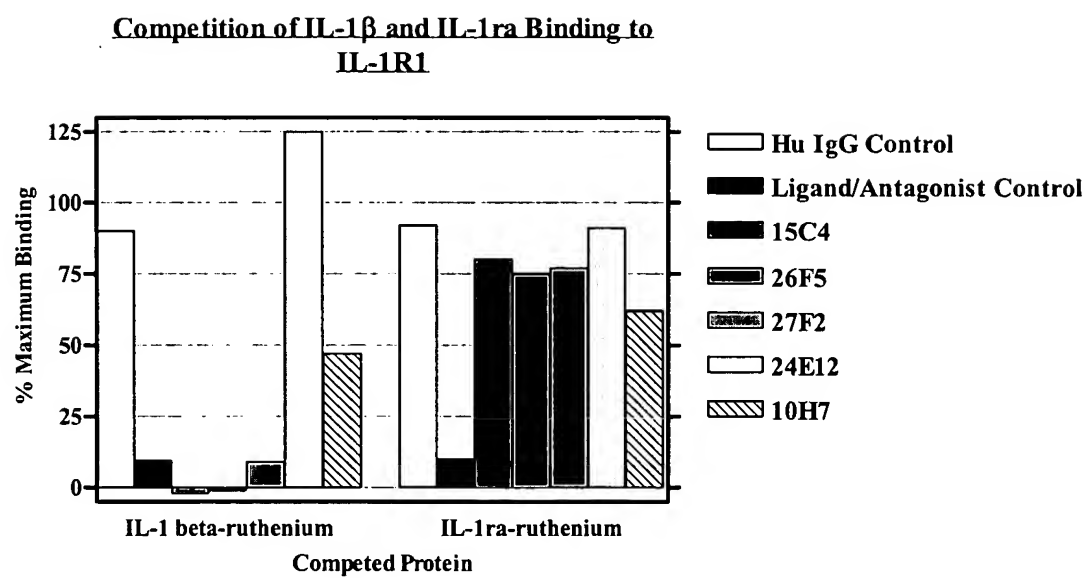


FIG. 15A

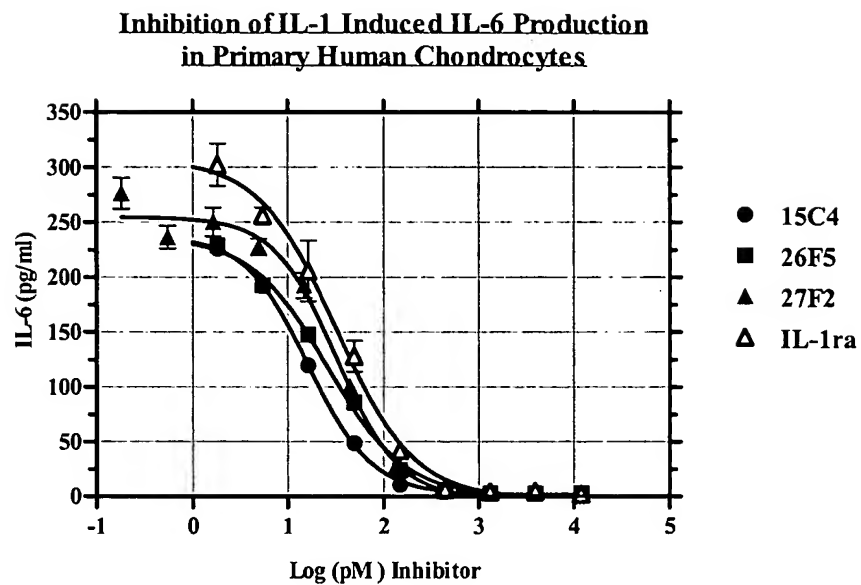


FIG. 15B

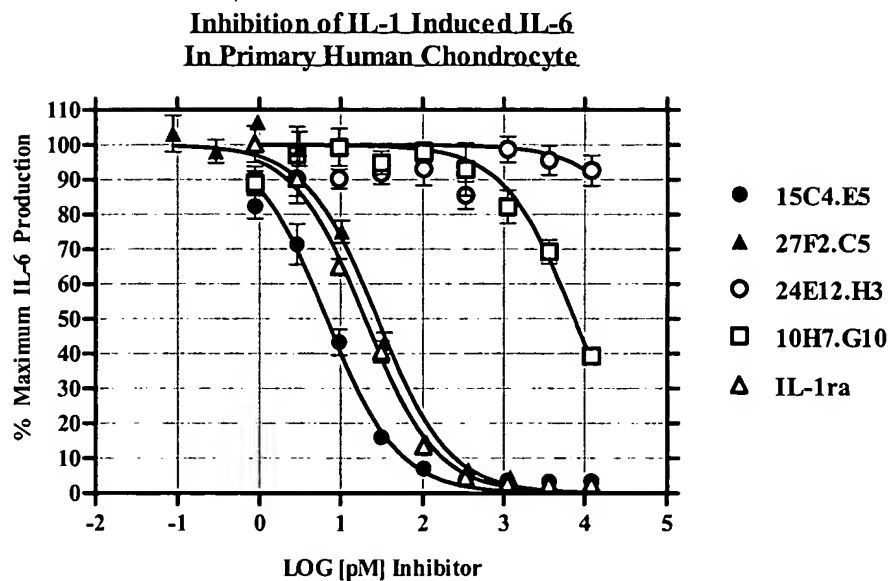
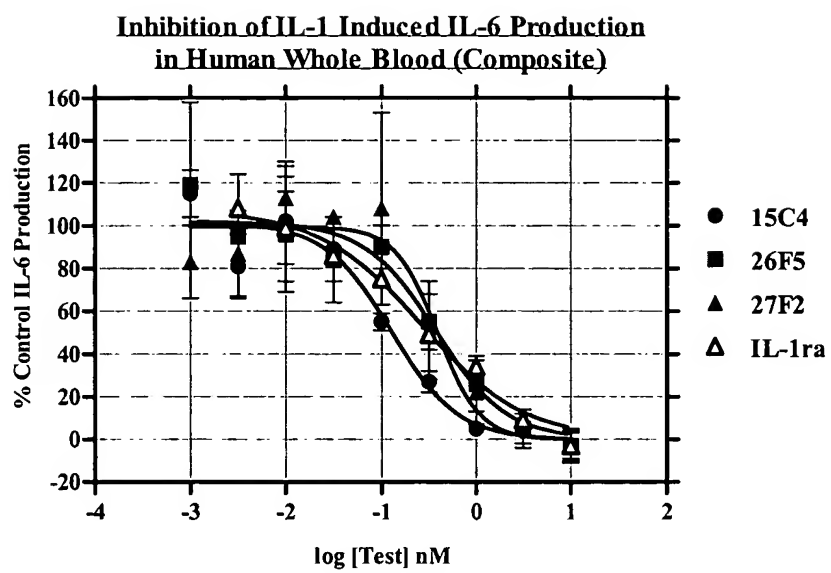


FIG. 16



hIL-1R

K336

S S S S S S

14

226 P V I V S P A N E T M E V D L G S 807

758 cctgtgattgtgagcccagctaatgagacaatggaagtagacttgggattc 807

1048 cctgtgattatgagcccaggaatgagacgatggaagctgaccaggattc 1097

15 M R A P 1

Q I Q L I C N V T G Q L S D I A Y

808 ccgatacaattgatctgtaatgtcacggccagttgagtgcatttgctt 857

1098 cagatacaactgatctgcaacgtcacggccagttcacgcacctgtct 1147

T F T L 3 V

2

W K W N G S V I D E D D P V L G

858 actggaagtggaatgggtcagtaattgatgaagatgaccagtgctaggg 907

1148 actggaagtggaatgggtcggaaattgaatgggacgatccaatcctagcc 1197

E E W I A

4 5 6

E D Y Y S V E N P A N K R R S T L

908 gaagactattacagtgtggaaaatcctgcaaaacaaaagaaggagtaccct 957

1198 gaagactatcagtttttggaaacaccttcagccaaaagaagtacactct 1247

Q 7 F L H S A 8 K Y 9

I T V L N I S E I E S R F Y K H P

958 catcacagtgtcttaatatatcggaattgaaagtagattttataaacatc 1007

1248 cattacaacacttaacgtttcagagggtcaaaagccagttttatcgctatc 1297

T 10 V V K Q 11 R Y

F T C F A K N T H G I D A A Y I

1008 catttacctgttttgccaagaatacacatggtatagatgcagcatatattc 1057

1298 cgttcatctgcttcgttaagaacactcatattctggagactgcacacgta 1347

I V I L E T H V

12 13.1

Q L I Y P V T N F Q K336 tm domain begins

1058 cagttaatatatccagtcactaatttcagaagcacatgattggtatatg 1107

1348 cggtagtataccagtttctgacttcaagaattacctcatcgggggctt 1397

R V P D K tm domain begins

FIG. 18

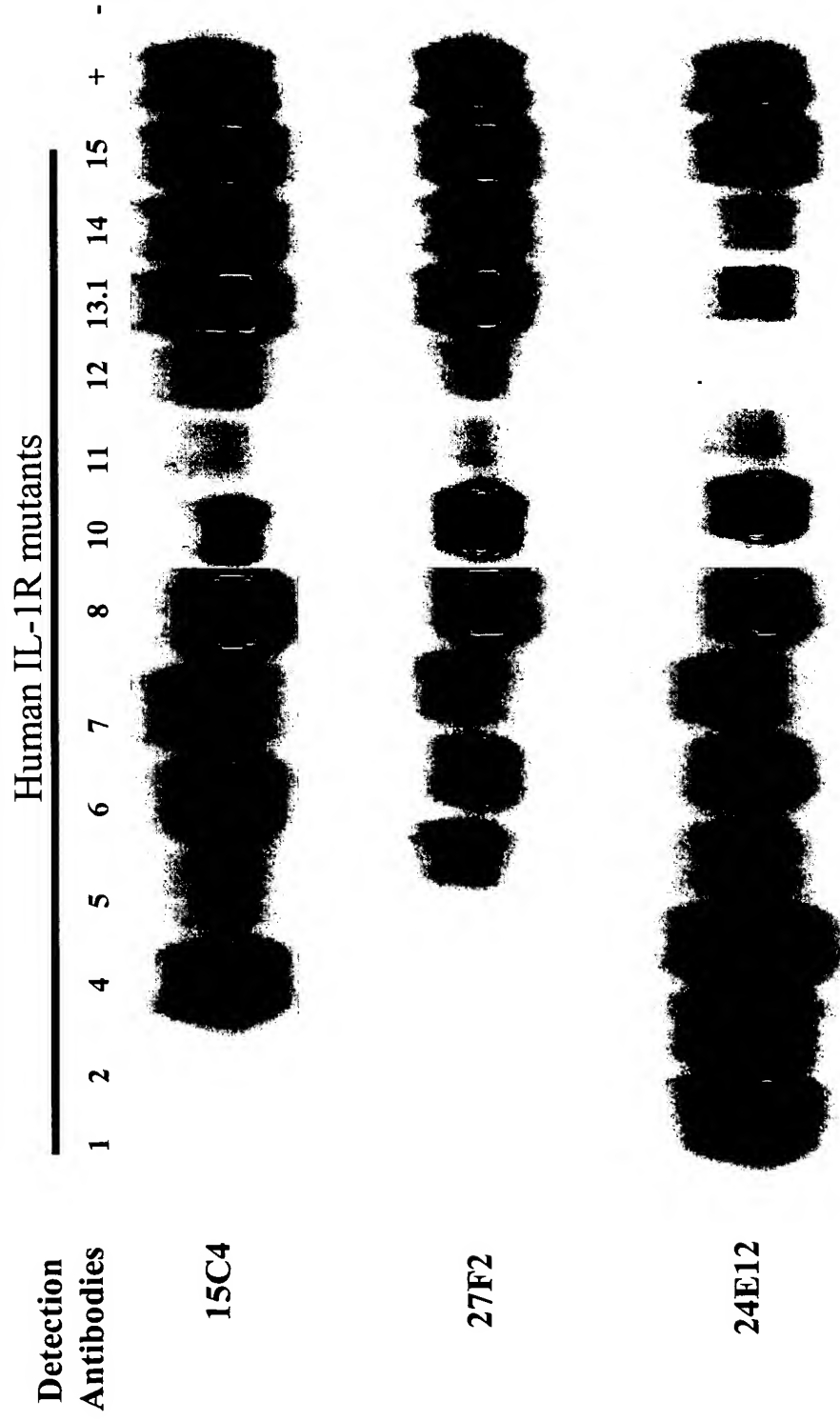


FIG. 19

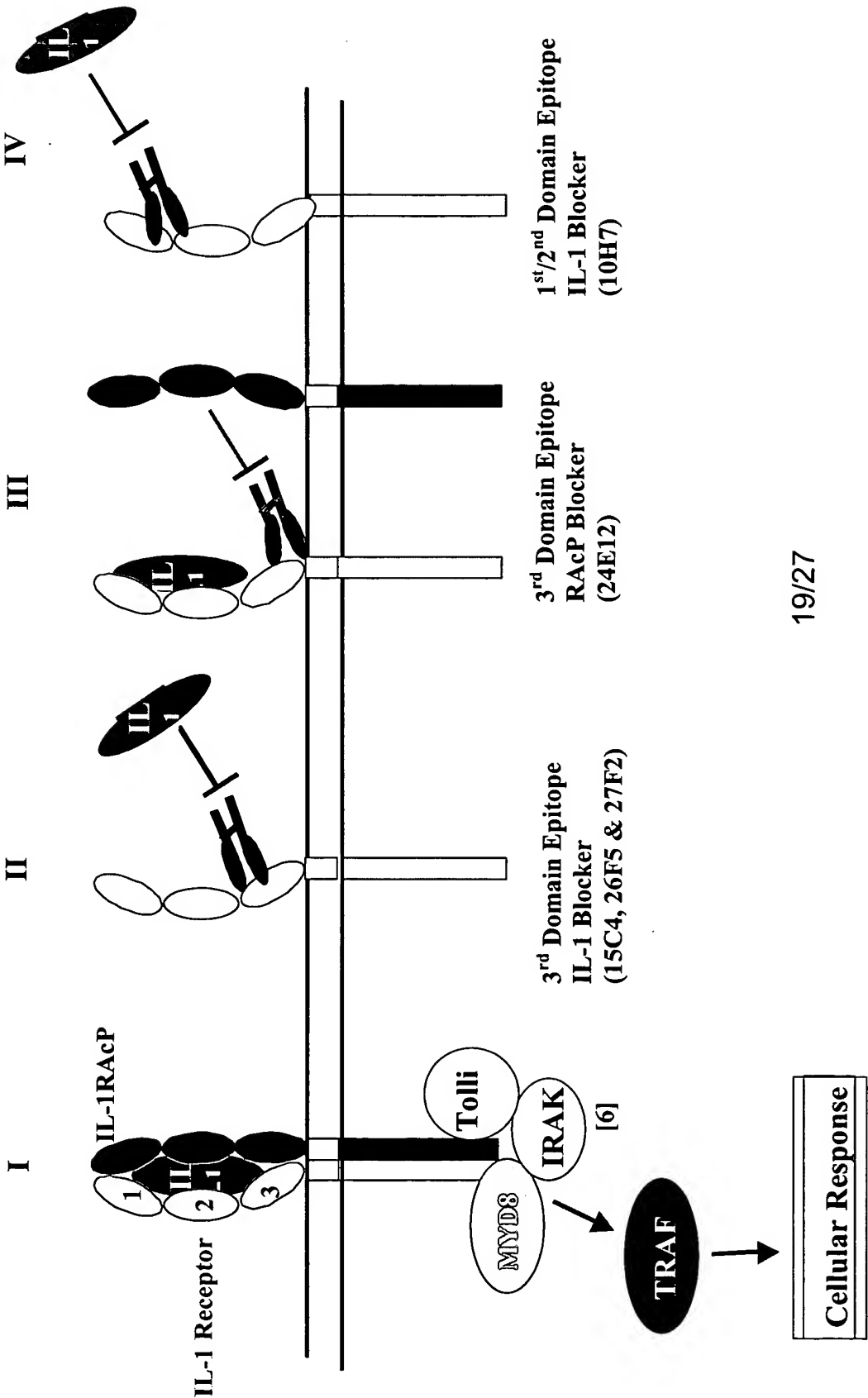


FIG. 20



FIG. 21

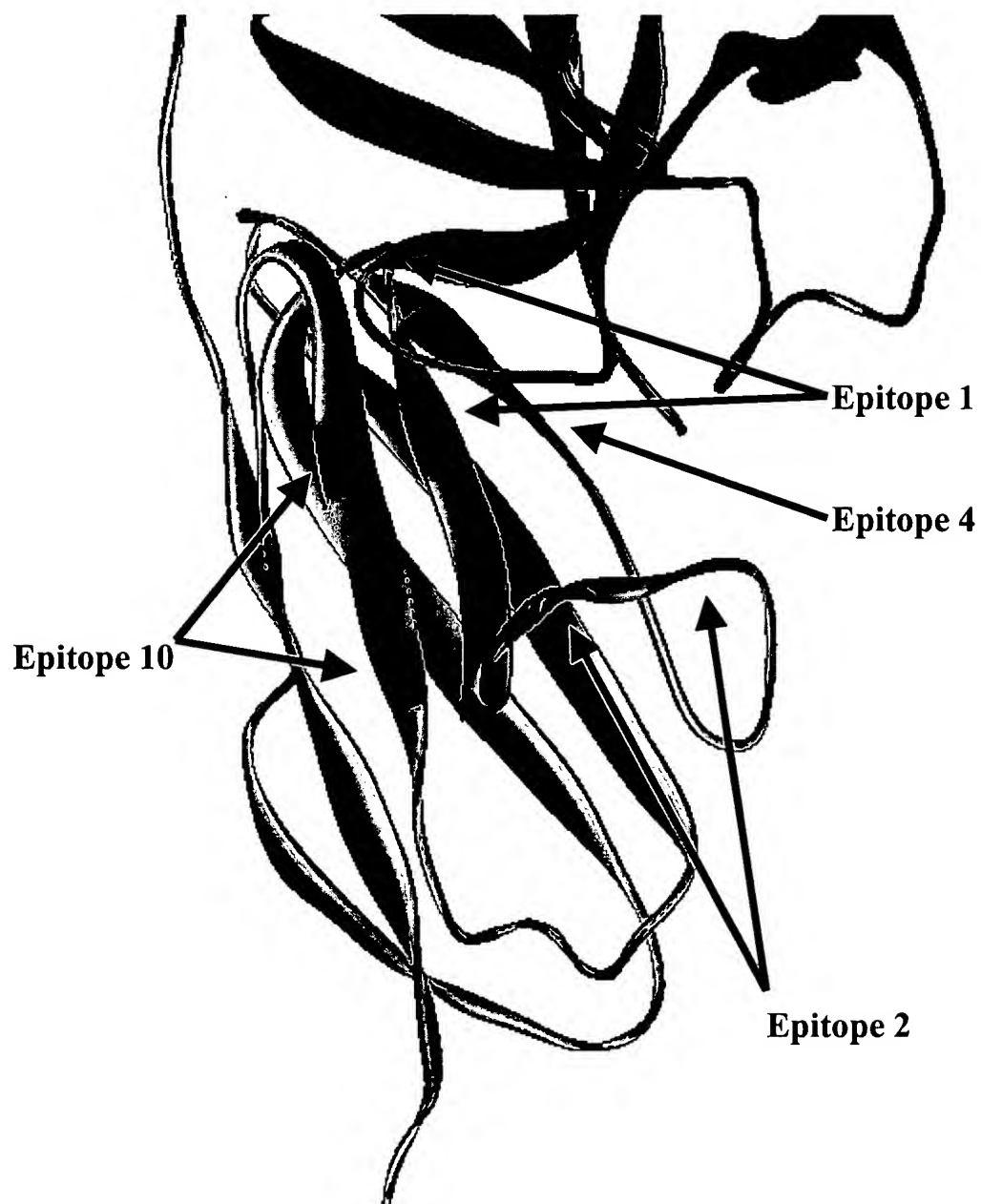


FIG. 22

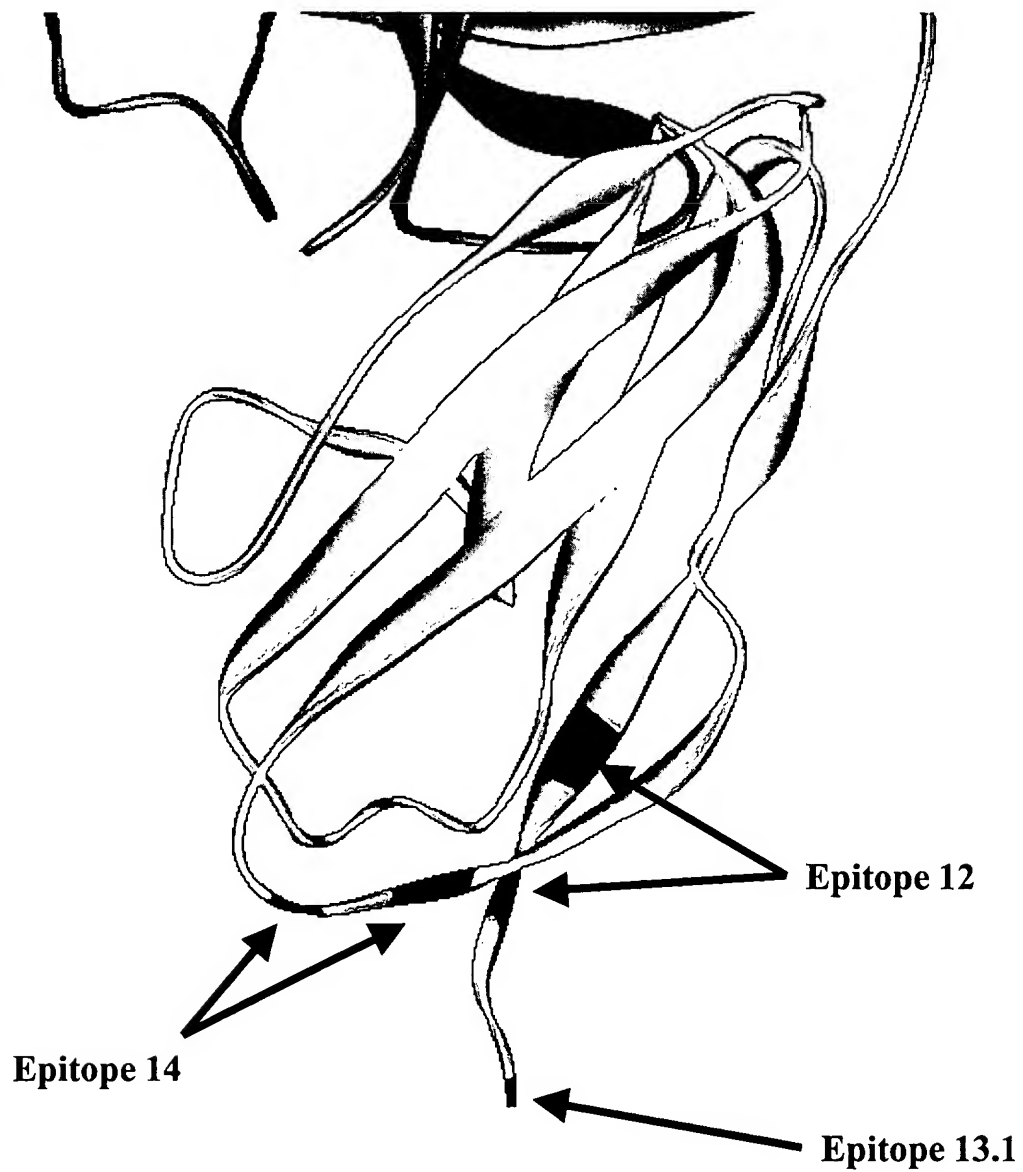


FIG. 23

MVHATSPLLL	LLLLSLALVA	PGLSARKCSL	TGKWTNDLGS	NMTIGAVNSK	GEFTGTYTTA	60
VTATSNEIKE	SPLHGTQNTI	NKRTQPTFGF	TVNWKFSEST	TVFTGQCFID	RNGKEVLKTM	120
WLLRSSVNDI	GDDWKATRVG	INIFTRLRTQ	KEQLLASLLE	ADKCKEREK	IILVSSANEI	180
DVRPCPLNPN	EHKGTITWYK	DDSKTPVSTE	QASRIHQHKE	KLWFVPAMVE	DSGHYYCVVR	240
NSSYCLRIKI	SAKFVENEPN	LCYNAQAIFK	QKLPVAGDGG	LVCPYMEFFK	NENNELPKLQ	300
WYKDCKPLLL	DNIHFSGVKD	RLIVMNVAEK	HRGNYTCHAS	YTYLGKQYPI	TRVIEFITLE	360
ENKPTRPVIV	SPANETMEVD	LGSQIQLICN	VTGQLSDIAY	WKWNGSVIDE	DDPVLGEDYY	420
SVENPANKRR	STLITVLNIS	EIESRFYKHP	FTCFAKNTHG	IDAAYIQLIY	PVTNFKDYK	480
DDDDK						485

FIG. 24

1 MVHATSPLLL LLLLSLALVA PGLSARKCSL TGKWTNDLGS NMTIGAVNSK GEFTGTYTTA

61 VTATSNEIKE SPLHGTQNTI NKRTQPTFGF TVNWKFESEST TVFTGQCFID RNGKEVLKTM

121 WLLRSSVNDI GDDWKATRVG INIFTRLRTQ KEQLLASLLE ADKCNEREK IILVSSANEI

181 DVRPCPLNPN EYKGTITWYK NDSKTIPISTE QASRIHQHKK KLWFVPAKVE DSGHYVCVVR

241 NSSYCLRIKI TAKFVENEPN LCYNAAEAFK QRLPVAGDGG LVCPYMEFFK DENNELPKLL

301 WYKDCKPLLL DNIHFSGVKD RLIVMNVAEK HRGNYTCHAS YTYLGKQYPI TRVIEFITLE

mutation 1 mutation 2

361 ENKPTRPVIV SPANETIEVD LGSQIQLICN VTGQLSDTAY WKWNGSFIDE DDPVLGEDYY
human **I** **V**

mutation 10.1 mutation 10.2

421 SVENPANKRR STLITVLNIS ETESRFYKHP FTCLARNTHG MDAAYVQLIY PVTKFQKD**YK**
human **F** **K**

481 **DDDDK**

FIG. 25A

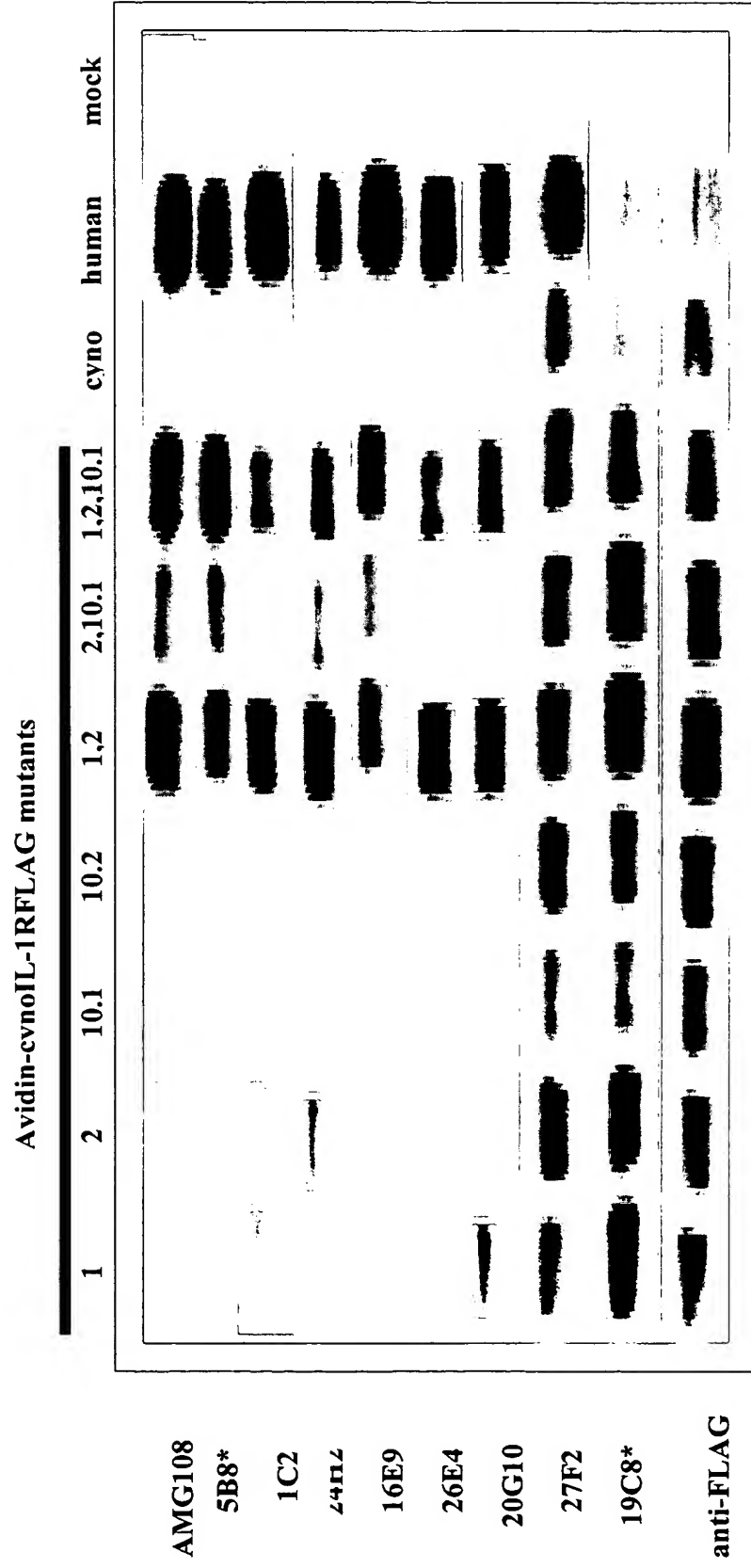
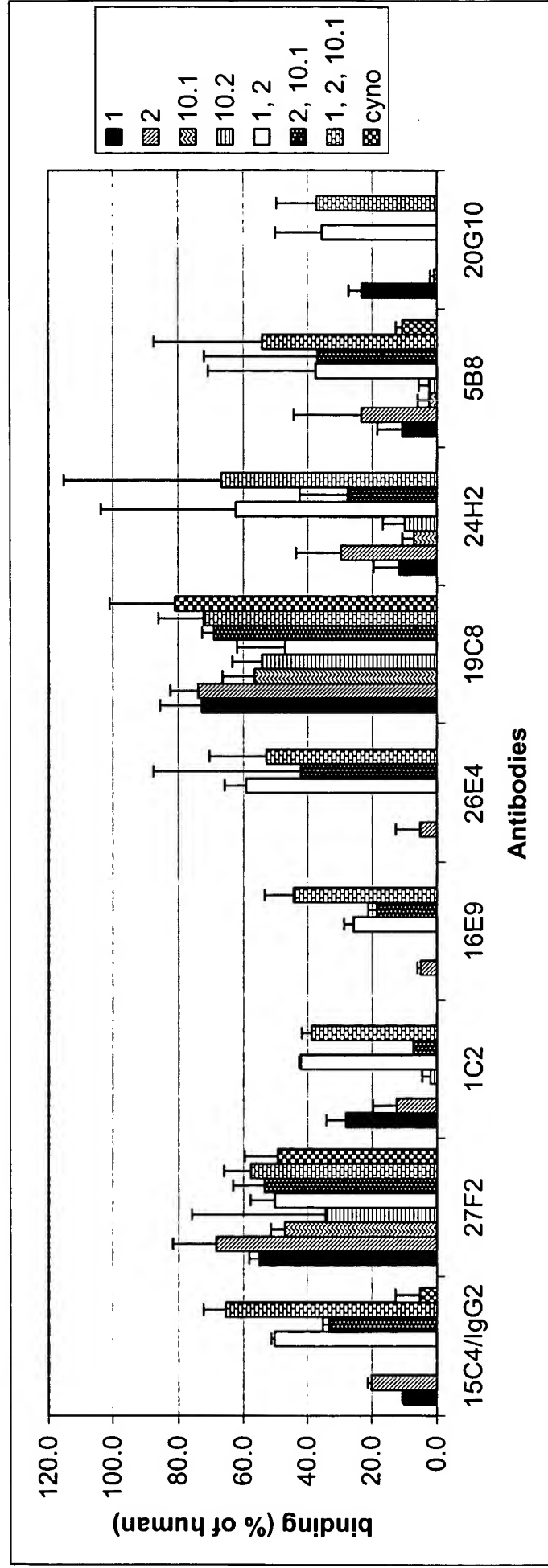


FIG. 25B



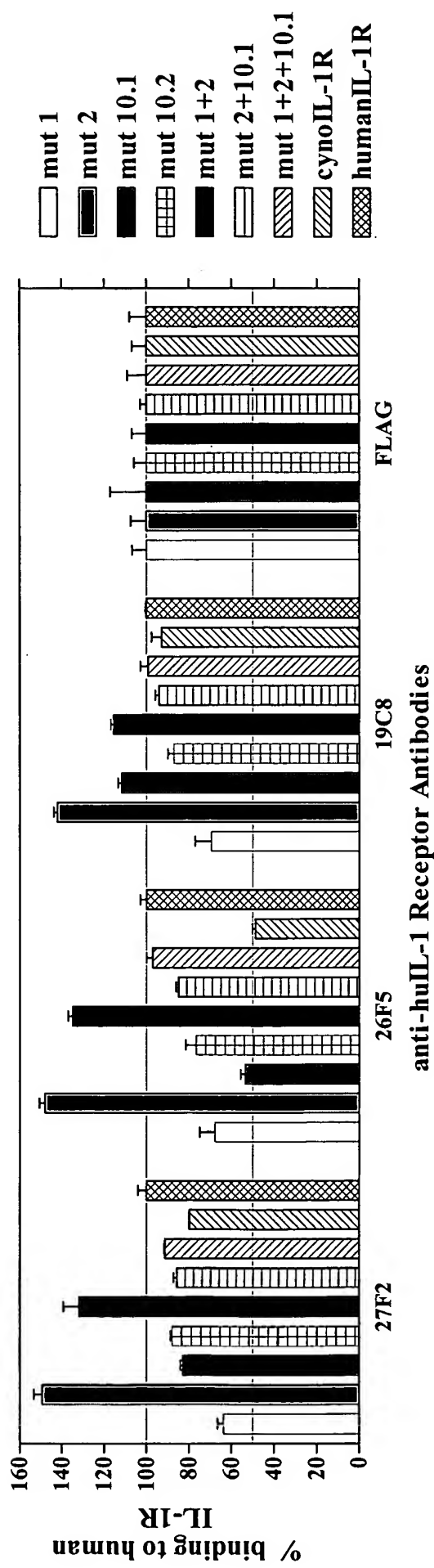
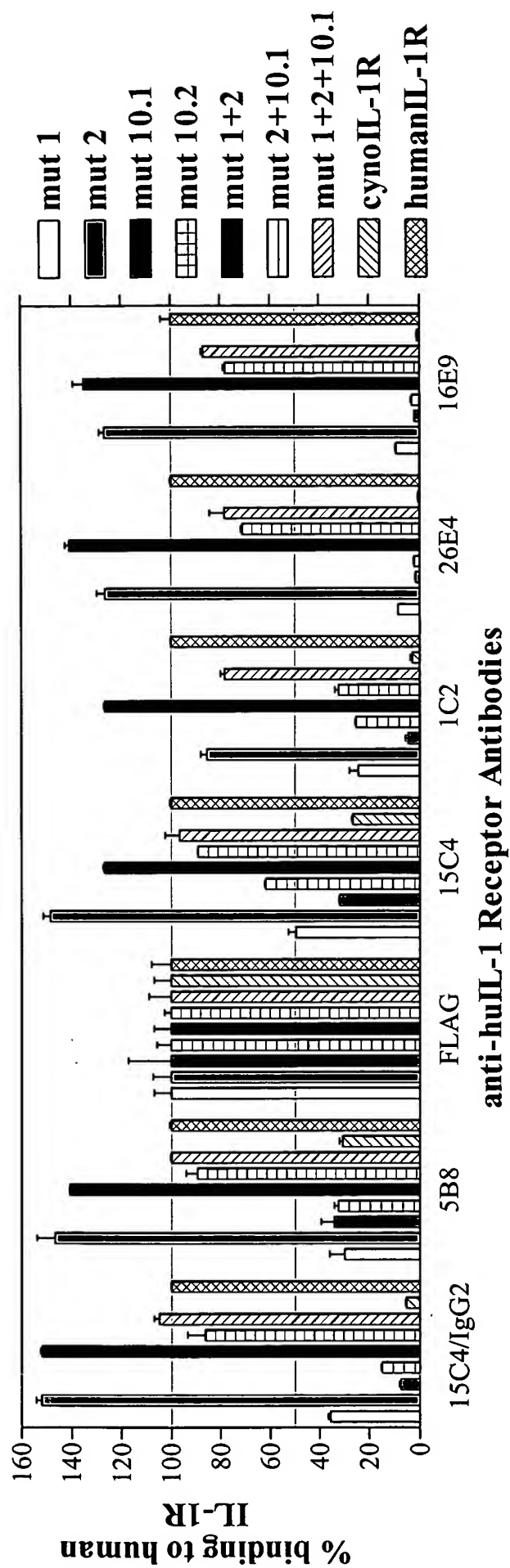


FIG. 26